PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 12 August 1997 (12.08.97)	
International application No. PCT/US96/18796	**Applicant's or agent's file reference** 228-049 PCT
International filing date (day/month/year) 21 November 1996 (21.11.96)	**Priority date** (day/month/year) 22 November 1995 (22.11.95)
Applicant PASCUAL, David et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   05 June 1997 (05.06.97)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

B. Fitzgerald

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

COMMUNICATION OF
INTERNATIONAL APPLICATIONS

(PCT Article 20)

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as designated Office

Date of mailing:
31 July 1997 (31.07.97)

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:	International publication no.:
PCT/US96/18796	WO97/18790

CORRECTED VERSION
VERSION CORRIGEE

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

09/068935

PK 5610

20

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 228-049 PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US96/18796	International filing date *(day/month/year)* 21 NOVEMBER 1996	Priority date *(day/month/year)* 22 NOVEMBER 1995
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE RESEARCH AND DEVELOPMENT INSTITUTE, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

CORRECTED VERSION

Date of submission of the demand 05 JUNE 1997	Date of completion of this report 02 MARCH 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer LILA FEISEE Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (January 1994)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

[X] the international application as originally filed.

[X] the description, pages 1-82 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.

[X] the claims, Nos. 1-54 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

[X] the drawings, sheets/~~fig~~ 1-2 , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[X] the description, pages NONE.
[X] the claims, Nos. NONE.
[X] the drawings, sheets/~~fig~~ NONE.

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 9-33, 37, 40, 42-46, 49

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. (See Attached).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. CITATIONS AND EXPLANATIONS

(See Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(6): A61K 35/12, 35/66; 38/17, 39/02; C07K 2/00, 4/04, 4/12 and US Cl.: 424/184.1, 520; 435/243; 514/ 2, 8; 530/300, 350

III. NON-ESTABLISHMENT OF REPORT:

No international search report has been established for claim numbers 9-33, 37, 40, 42-46, 49.

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 50-54.
The report as to Novelty was negative (NO) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48.
The report as to Inventive Step was positive (YES) with respect to claims NONE.
The report as to Inventive Step was negative (NO) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Explanations

Claims 1-8, 34-36, 38, 39, 41, 47, 48 and 50-54 are under consideration as E-selectin, as drawn to the first invention under Unity of Invention.

Claims 1-8, 34-36, 38, 39, 41, 47, 48 lack novelty under PCT Article 33(2) as being clearly anticipated by Bevilacqua et al. (U.S. Patent No. 5.081,034; see entire document). Bevilacqua et al. teach ELAM-1 and fragments thereof in pharmaceutical compositions to treat various disorders including the treatment of microbial infections (columns 13-14) as well as diagnostic assays to detect ELAM-1 with specific antibodies (columns 10-12). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced ELAM-1-specific compositions and assays.

Claims 1-8, 34-36, 38, 39, 41, 47, 48 lack novelty under PCT Article 33(2) as being clearly anticipated by Centocor, Inc. (WO 94/05269; see entire document). Centocor, Inc. teach E-selectin pharmaceutical compositions to treat various disorders including the treatment of bacterial sepsis (pages 19-22) as well as diagnostic assays to detect ELAM-1 with specific antibodies (pages 22-23). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced E-selectin-specific compositions and assays.

Claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54 lack an inventive step under PCT Article 33(3) as being obvious over Bevilacqua et al. (U.S. Patent No. 5.081,034) or Centocor, Inc. (WO 94/05269) in view of Biocarb, Inc. (WO 92/02817) and Sandros et al. (Glycoconjugate Journal, 1994).

Bevilacqua et al. (see entire document) teach ELAM-1 and fragments thereof in pharmaceutical compositions to treat various disorders including the treatment of microbial infections (columns 13-14) as well as diagnostic assays to detect ELAM-1 with specific antibodies (columns 10-12).

Centocor, Inc. (see entire document) teach E-selectin pharmaceutical compositions to treat various disorders including the treatment of bacterial sepsis (pages 19- 22) as well as diagnostic assays to detect ELAM-1 with specific antibodies (pages 22-23).

Biocarb, Inc. (see entire document) teach the importance of adhesion molecules in microbial colonization and infection and how to make and use receptors for pathogenic or opportunistic microorganisms, including diagnostics, therapeutic and vaccines (Summary of the Invention).

Sandros et al. teach that the pathogenesis of infectious diseases is critically determined by prokaryotic lectins which

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

recognize and activate targeted eukaryotic cells and that bacterial adhesion mimic and co-opt eukaryotic cell-cell adhesion motifs (see entire document, including the Abstract). Also, Sandros et al. teach that mimicry is sufficient to engender biological interference between prokaryotic and eukaryotic versions of selectin motifs and that strategies would employ utilizing bacterial variants of host selectins (see page 505, last paragraph).

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of E-selectin (or ELAM-1) -specific therapeutic and diagnostic agents or bacterial variants of said E-selectin-specific reagents to characterize eukaryotic-prokaryotic interactions as well as to develop diagnostic and therapeutic agents to detect and treat bacterial-related diseases associated with E-selectin. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's response, filed 1/22/98 (Paper No. 16), has been fully considered but not found convincing. Applicant acknowledges that the references do teach ELAM-1 and E-selectin and fragments thereof. However, applicant argues that none of the references disclose vaccines of the present invention which are capable of binding to a molecular address on the host cell and capable of trigerrig one or more signal transduction pathways and enabling a selected pathogen or its toxin to traffic through host tissue. Applicant argues that the claims are broader than realized by the prior art and that the purpose of the claimed invention differs from the prior art. However, the intended use and the breadth of the instant claims do not obviate the anticipatory prior art over the same products and methods. In addition, the prior art does provide motivation and an expectation of success in practicing the products and methods encompassed by the claims for the reasons set forth above..

---------- NEW CITATIONS ----------

NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 228-049 PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US96/18796	International filing date *(day/month/year)* 21 NOVEMBER 1996	Priority date *(day/month/year)* 22 NOVEMBER 1995
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE RESEARCH AND DEVELOPMENT INSTITUTE, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of — sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05 JUNE 1997	02 MARCH 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PAULA HUTZELL Telephone No. (703) 308-0196

Form PCT/IPEA/416 (cover sheet) (January 1994)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

[X] the international application as originally filed.

[X] the description, pages 1-82 , as originally filed.
pages NONE , filed with the demand.
pages NONE , filed with the letter of _____.
pages _____ , filed with the letter of _____.

[X] the claims, Nos. 1-54 , as originally filed.
Nos. NONE , as amended under Article 19.
Nos. NONE , filed with the demand.
Nos. NONE , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

[X] the drawings, sheets/~~fig~~ 1-2 , as originally filed.
sheets/~~fig~~ NONE , filed with the demand.
sheets/~~fig~~ NONE , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[X] the description, pages NONE .
[X] the claims, Nos. NONE ,
[X] the drawings, sheets/~~fig~~ NONE ,

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 9-33, 37, 40, 42-46, 49

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. (See Attached).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US96/18796

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. CITATIONS AND EXPLANATIONS

(See Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(6): A61K 35/12, 35/66; 38/17, 39/02; C07K 2/00, 4/04, 4/12 and US Cl.: 424/184.1, 520; 435/243; 514/ 2, 8; 530/300, 350

III. NON-ESTABLISHMENT OF REPORT:

No international search report has been established for claim numbers 9-33, 37, 40, 42-46, 49 .

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 50-54.
The report as to Novelty was negative (NO) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48.
The report as to Inventive Step was positive (YES) with respect to claims NONE.
The report as to Inventive Step was negative (NO) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Explanations

Claims 1-8, 34-36, 38, 39, 41, 47, 48 and 50-54 are under consideration as E-selectin, as drawn to the first invention under Unity of Invention.

Claims 1-8, 34-36, 38, 39, 41, 47, 48 lack novelty under PCT Article 33(2) as being clearly anticipated by Bevilacqua et al. (U.S. Patent No. 5.081,034; see entire document). Bevilacqua et al. teach ELAM-1 and fragments thereof in pharmaceutical compositions to treat various disorders including the treatment of microbial infections (columns 13-14) as well as diagnostic assays to detect ELAM-1 with specific antibodies (columns 10-12). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced ELAM-1-specific compositions and assays.

Claims 1-8, 34-36, 38, 39, 41, 47, 48 lack novelty under PCT Article 33(2) as being clearly anticipated by Centocor, Inc. (WO 94/05269; see entire document). Centocor, Inc. teach E-selectin pharmaceutical compositions to treat various disorders including the treatment of bacterial sepsis (pages 19-22) as well as diagnostic assays to detect ELAM-1 with specific antibodies (pages 22-23). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced E-selectin-specific compositions and assays.

Claims 1-8, 34-36, 38, 39, 41, 47, 48, 50-54 lack an inventive step under PCT Article 33(3) as being obvious over Bevilacqua et al. (U.S. Patent No. 5.081,034) or Centocor, Inc. (WO 94/05269) in view of Biocarb, Inc. (WO 92/02817) and Sandros et al. (Glycoconjugate Journal, 1994).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Bevilacqua et al. (see entire document) teach ELAM-1 and fragments thereof in pharmaceutical compositions to treat various disorders including the treatment of microbial infections (columns 13-14) as well as diagnostic assays to detect ELAM-1 with specific antibodies (columns 10-12).

Centocor, Inc. (see entire document) teach E-selectin pharmaceutical compositions to treat various disorders including the treatment of bacterial sepsis (pages 19- 22) as well as diagnostic assays to detect ELAM-1 with specific antibodies (pages 22-23).

Biocarb, Inc. (see entire document) teach the importance of adhesion molecules in microbial colonization and infection and how to make and use receptors for pathogenic or opportunistic microorganisms, including diagnostics, therapeutic and vaccines (Summary of the Invention).

Sandros et al. teach that the pathogenesis of infectious diseases is critically determined by prokaryotic lectins which recognize and activate targeted eukaryotic cells and that bacterial adhesion mimic and co-opt eukaryotic cell-cell adhesion motifs (see entire document, including the Abstract). Also, Sandros et al. teach that mimicry is sufficient to engender biological interference between prokaryotic and eukaryotic versions of selectin motifs and that strategies would employ utilizing bacterial variants of host selectins (see page 505, last paragraph).

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of E-selectin (or ELAM-1) -specific therapeutic and diagnostic agents or bacterial variants of said E-selectin-specific reagents to characterize eukaryotic-prokaryotic interactions as well as to develop diagnostic and therapeutic agents to detect and treat bacterial-related diseases associated with E-selectin. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

---------- NEW CITATIONS ----------
NONE

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/18796

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 35/12, 35/66; 38/17, 39/02; C07K 2/00, 4/04, 4/12
US CL :424/184.1, 520; 435/243; 514/ 2, 8; 530/300, 350
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/184.1, 520; 435/243; 514/ 2, 8; 530/300, 350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, DIALOG, BIOSIS, CA, EMBASE, MEDLINE, WPI
search terms: elam, e-selectin, bacteri?, microorganism?, mimic?

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,081,034 A (BEVILACQUA et al.) 14 January 1992, see entire document.	1-8, 34-36, 38, 39, 41, 47,48 ---------- 50-54
X --- Y	WO 94/05269 A1 (CENTOCOR, INC.) 17 March 1994, see entire document.	1-8, 34-36, 38, 39, 41, 45, 47, 48 ---------- 50-54
X --- Y	WO 92/02817 A1 (BIOCARB, INC.) 20 February 1992, see entire document.	50-54 ---------- 1-8, 34-36, 38, 39, 41, 45, 47, 48

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 MARCH 1997	09 JUN 1997

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	PHILLIP GAMBEL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/18796

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Glycoconjugate Journal, Volume 11, issued 1994, SANDROS et al., "Lectin Domains in the Toxin of Bordetella Pertussis: Selectin Mimicry Linked to Microbial Pathogenesis", pages 501-506, see entire document.	1-8, 34-36, 38, 39, 41, 45, 47, 48

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/18796

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-8, 34-36, 38, 39, 41, 45, 47, 48, 50-54

Remark on Protest

☒ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/18796

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. The special technical feature of the instant application is an attachment molecule including proteins and glyconjugates or a member of a receptor-ligand pair (e.g. adhesion molecule, cytokine, etc.). The disclosed and claimed attachment molecules were known in the prior art as evidenced by Ward et al. (Agents Action 43/Suppl. 173-186, 1993); therefore the multiple species of attachment molecules do not have unity of invention.

I. This application contains claims directed to the following distinct species, wherein the attachment molecule is selected from the group consisting of:(1)proteins, glycoproteins, (2) glycolipids or (3) carbohydrates.

These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

II. This application contains claims directed to the following distinct species, wherein the targeted host cells for an attachment molecule is selected from the group consisting of:
(1)leukocytes, (2)endothelial cells, (3)epithelial cells, or (4) cells of the nervous system. These species do not share the same or corresponding special technical feature because these species are distinct because these targeted structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

III. In addition to choosing a targeted cell type, this application contains claims directed to the following distinct species, wherein the targeted ligand is selected from the group consisting of:(1)N-acetylneuraminic acid, (2)sialic acid, (3) N-acetylglucosamine or glucosamine, (4)N-acetylgalactosamine or galactosamine, (5)galactose, (6)mannose, (7)fucose or (8) lactose.

These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

IV. If applicant elects a protein/glycoprotein, this application contains claims directed to the following distinct species, wherein the attachment molecule is selected from the group consisting of: (1)selectin or integrin,(2)cytokine, (3) chemokine, or (4)GTP-binding protein.
These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

V. If applicant elects a GTP-binding protein, this application contains claims directed to the following distinct species, wherein the attachment molecule is selected from the group consisting of: (1)Rho, (2)Ras, (3)Rac, (4)Cdc42, (5)Rab, (6)Ran or (7) Arf.

These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

VI. If applicant elects a selectin/integrin then this application contains claims directed to the following distinct species, wherein the attachment molecule is selected from the group consisting of: (1)E-selectin, (2)P-selectin, (3)L-selectin, (4)VLA-1, (5)VLA-2, (6)VLA-3, (7)VLA-4, (8)VLA-5, (9) VLA-6, (10)Mac-1, (11)LFA-1, (12)gp150.95, (13)CD41a, (14)CD49, (15)CD51, (16)ICAM-1, (17)ICAM-2, (18)ICAM-3, (19)VCAM, (20) NCAM or (21)PECAM.

These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn, address different pathological conditions and therapeutic endpoints.

VII. This application contains claims directed to the following distinct species, wherein the attachment molecule is selected from the group consisting of the microbes selected from the group of:(1) E. coli, (2) Salmonella, (3) Shigella, (4) Pseudomonas, (4) Proteus, (5) Klebsiella, (6) Aerobacter, (7) Heliobacter, (8) Plasmodium, (9) Brucella, (10) Pasteurella, (11) Leishmania, (12) Trypanosoma, (13) Mycobacterium TB, (14) Legionella, (15) Staphylococcus, (16) Streptococcus, (17) Bordetella, (18) Hemophilus, (19), Aspergillus, (20) Cryptococcus, (21) Candida, (22) Histoplasma,

(23) Coccidioides, (24) Phycomycetes, (25) Entamoeba, (26) Giardia, (27) Cryptosporidium, (28) Neisseria, (29) Chlamydia, (30) Treponema, (31) Trichomona, (32) Tritrichomonas, (33) Influenza A, (34) Influenza B, (35) Influenza C, (36) Measles, (37) Mumps, (38) Adenovirus, (39) Rhinovirus, (40), Poliovirus, (41) Hepatitis, (42) Hantavirus, (43) Herpesvirus, (44) Rubella, (45) HIV, Coxsackievirus, (46) Corynebacterium, (47) Clostridium, (48) Yersinia, (49) Vibrio, (50) Entamoeba or (51) Hafnia.

These species do not share the same or corresponding special technical feature because these species are distinct because their structures and modes of action are different which, in turn,address different pathological conditions and therapeutic endpoints.

Applicant should elect a species from (I), (II) and (VII) as a single group and in addition, select an additional species from (III), (IV), (V) or (VI) as appropriate.

NP 5/22/98

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 35/12, 35/66, 38/17, 39/02, C07K 2/00, 4/04, 4/12

A3

(11) International Publication Number: **WO 97/18790**

(43) International Publication Date: 29 May 1997 (29.05.97)

(21) International Application Number: PCT/US96/18796

(22) International Filing Date: 21 November 1996 (21.11.96)

(30) Priority Data:
60/007,477 22 November 1995 (22.11.95) US

(60) Parent Application or Grant
(63) Related by Continuation
US 60/007,477 (CON)
Filed on 22 November 1995 (22.11.95)

(71) Applicant *(for all designated States except US)*: THE RESEARCH AND DEVELOPMENT INSTITUTE, INC. [US/US]; 1711 West College, Montana State University, Bozeman, MT 59715 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: PASCUAL, David [US/US]; 8220 Indian Paint Brush Drive, Bozeman, MT 59178 (US). BOND, Clifford [US/US]; 9552 Cougar Drive, Bozeman, MT 59715 (US). BURRITT, James [US/US]; 1215 S. Bozeman, Bozeman, MT 59715 (US). BURGESS, Don [US/US]; 5553 Black Bear, Bozeman, MT 59715 (US). GLEE, Pati [US/US]; 813 W. Villard #75, Bozeman, MT 59718 (US). JUTILA, John [US/US]; 516 S. Grand Avenue, Bozeman, MT 59715 (US). JUTILA, Mark [US/US]; 3308 Sundance Drive, Bozeman, MT 59715 (US). BARGATZE, Robert [US/US]; 1302 Wildflower Way, Bozeman, MT 59715 (US). MCFETERS, Gordon [US/US]; 1320 Cherry Drive, Bozeman, MT 59175 (US). PYLE, Barry [NZ/US]; 4985 Foster Lane, Bozeman, MT 59175 (US). CUTLER, Jim, E. [US/US]; 1426 Ash Drive, Bozeman, MT 59715 (US). HAN, Yongmoon [US/US]; 306 Treasure Avenue, Bozeman, MT 59715 (US).

(74) Agents: PRICE, Robert, L. et al.; Lowe, Price, LeBlanc & Becker, Suite 300, 99 Canal Center Plaza, Alexandria, VA 22314 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
31 July 1997 (31.07.97)

(54) Title: THERAPEUTIC AND DIAGNOSTIC AGENTS FOR THE TREATMENT OF MICROBIAL INFECTIONS

(57) Abstract

Therapeutic peptides, vaccines and diagnostic agents for the treatment of pathogenic infections.